§312.23(9)(a)(iii) Radiation Dosimetry in Healthy Human Volunteers

§312.23(9)(a)(iii)(2) Methods: The final sample included 4 men and 6 women; 5 were Caucasian, 3 were African American, 1 was Hispanic, and 1 was Asian American. They had a mean age of 33.7 ±11.3 years (range:21-54). The 4 men had an average weight of 79.6 ± 7.2 kg (175 ± 16 lb.) and a mean height of 173.6 ± 4.7 cm (68.4 ± 1.9 inches). The 6 women weighed an average of 65.6 ± 1.9 kg (148 ± 17 lb.) and had a mean height of 167.5 ± 4.8 cm (65.6 ± 1.9 inches).

§312.23(9)(a)(iii)(3) Results: SPECT images showed selective localization in the basal ganglia of the brain and retention in the bone marrow of the skull. Planar images demonstrated differentially increased activity in the nasal mucosa, the stomach, and the testes.

Image analysis demonstrated that the radioactivity associated with TRODAT was relatively slow to penetrate the adipose tissues, an effect that was particularly noticeable in the lower extremities. It was excreted primarily by the liver. Image analysis of the urine specimens produced experimentally measured renal excretion fractions of 20.3 to 31.25% during the first 28 hours of study (mean ± SD: 25.2 ± 4.7%). Urine specimens obtained after 28 hours did not have any detectable activity in them. Most all of the remaining dose could be detected in the GI tract.

Radioactivity was taken up by the liver rapidly. The fraction of the dose in the liver then increased continuously, but minimally, on the initial images. It did not peak for more than 10 hours, after which the curves were essentially flat. Over 30% of the injected dose was still in the liver at the end of the study.

Activity in the left upper quadrant corresponding to the stomach could usually be seen on the very first whole body scans (Figure 4). During the next several hours, this activity became progressively more obscure. It could not be visualized at all once activity was excreted into the small bowel, and then the colon. Activity could be seen entering the cecum in less than 6 hours. Despite the rapidity with which activity entered the lumen of the colon, the decay corrected fecal excretion fraction never exceeded more than 10% during the first 28 hours, or more than 35% during the first 43 hours.

Residence Times: Calculations of the residence times in each organ showed that the effective half life of radioactivity associated with TRODAT was longest in the liver at 3.24 mCi-hours (range: 2.42-3.81). Of particular note was the mean residence time in the heart of only 0.19 hours (maximum = 0.31 hours).

Radiation Absorbed Doses (RADs): Table 2 lists the absorbed dose estimates for the entire sample. The differences between men and women were minimal when compared to the variability within each group. The dose limiting organ in both sexes was the liver, which received an estimated 0.046 mGy/MBq (0.17 rads/mCi). For female subjects, five organs were estimated to receive mean absorbed doses higher than 0.080 rad/mCi (liver, 0.19 rad/mCi; kidneys, 0.13 rad/mCi; ULI, 0.11 rad/mCi; spleen, 0.095 rad/mCi; and bladder wall, 0.082 rad/mCi). The maximum organ absorbed dose for any female subject was 0.22 rad/mCi to the liver. The variability in organ absorbed doses was reasonable with only two organs showing percent standard deviations above 30% (thyroid and spleen). These organs were not well visualized on the images, and were based on estimates from stylized ROIs. In the case of the spleen, like that of the kidneys, it was not possible to keep the measurements from being confounded by the activity sweeping by in first the small bowel and then the splenic flexure of the colon. Substantially less variability was associated with the mean effective dose equivalent and effective dose, which were 0.059 rem/mCi and 0.049 rem/mCi, respectively.